

FILE 'HOME' ENTERED AT 15:53:42 ON 04 JAN 2002}

FILE 'BIOSIS, EMBASE, CAPLUS, MEDLINE, CANCERLIT' ENTERED AT 15:55:00 ON
04 JAN 2002

L1 80614 S GENE THERAP?
L2 224 S L1 AND CIRRHOSIS
L3 123566 S LIVER CELL?
L4 32 S L3 AND RETROVIRAL TRANSDUCTION
L5 0 S L2 AND L4
L6 5713 S (KERATINOCYTE GROWTH FACTOR? OR KGF)
L7 68010 S (TRI-ICDOTHYRONINE OR TRIICDOTHYRONINE)
L8 8 S L6 AND L7
L9 0 S L8 AND L2
L10 101 S DIOCTADECYLAMIDOGLYCYLSFERMINE
L11 0 S L10 AND L4
L12 2 S L10 AND L8
L13 1 DUP REM L12 (1 DUPLICATE REMOVED)

118 1 ti abs ibib

118 ANSWER 1 OF 1 MEDLINE

DUPLICATE 1

TI Synergistic growth factors enhance rat liver proliferation and enable retroviral gene transfer via a peripheral vein.

AB BACKGROUND & AIMS: Genetic diseases reflecting abnormal hepatocyte function are potentially curable through gene therapy. Retroviral vectors offer the potential for permanent correction of such conditions. These vectors generally require cell division to occur to allow provirus entry into the nucleus, initiated in many experimental protocols by partial hepatectomy. We have explored methods to improve the efficiency of retroviral gene transfer that avoid the need for liver damage. METHODS:

Triiodothyronine (T3) and keratinocyte growth

factor (KGF) were used to induce hepatic proliferation

in rats. The effects of intraportal and peripheral administration of a modified retrovirus that encoded the Lac Z gene during growth

factor-induced liver hyperplasia were analyzed. RESULTS: T3 initiated

hepatocyte proliferation midzonally; after **KGF**, proliferation

was more diffuse. Optimal concentrations of T3 and **KGF** acted

synergistically to induce proliferation in 61% of hepatocytes in the

intact liver. This enabled in vivo hepatocyte transduction, leading to

gene expression by up to 7.3% of hepatocytes after intraportal retroviral

vector administration and 7.1% after peripheral venous administration.

CONCLUSIONS: T3 and **KGF** act synergistically to induce hepatocyte

proliferation in undamaged liver. The liver can be simply transduced with

integrating vectors via the peripheral venous system during a wave of

growth factor-induced proliferation.

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